REMARKS

Reconsideration of this Application and entry of these Amendments is respectfully requested. By the amendments, Applicants do not acquiesce to the propriety of any of the Examiner's rejections and do not disclaim any subject matter to which they are entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 U.S.P.Q.2d 1865 (U.S. 1997).

No new matter has been added as a result of the present amendments.

In the claims

Claims 1-20 and 29 are pending in this application.

Claims 1, 2, 9, 16, and 18 have been amended to further clarify the claimed subject matter. Support for these amendments can be found throughout the specification as filed, such as, for example, in paragraph 107 of the published application. Claims 4 and 17 have been canceled.

35 U.S.C. §112 Rejections

1) The Office Action rejects claims 1-20 and 29 under 35 USC 112, first paragraph, "because the specification, while being enabling for a method for treating acute pain medication overuse disorder comprising administering up to 260 units of botulinum toxin to a patient in need of such treatment does not reasonably provide enablement for a method for treating acute pain medication overuse disorder comprising administering about 3000 units of botulinum toxin of any serotype (including serotype A) made by any manufacturer to a patient in need of such treatment.." *See* Office Action at p3. The Applicants respectfully disagree, and direct the Examiner's attention to MPEP 2164, specifically the following passage:

> The information contained in the disclosure of an application must be sufficient to inform those skilled in the relevant art how to both make and use the claimed invention. However, to comply with 35 U.S.C. 112, first paragraph, it is not necessary to "enable one of ordinary skill in the art to make and use a perfected, commercially viable embodiment absent a claim limitation to that effect." *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1338, 68 USPQ2d 1940,

> 1944 (Fed. Cir. 2003) (an invention directed to a general system to improve the cleaning process for semiconductor wafers was enabled by a disclosure showing improvements in the overall system). Detailed procedures for making and using the invention may not be necessary if the description of the invention itself is sufficient to permit those skilled in the art to make and use the invention.

In light of the quoted MPEP guidance, the Applicants believes that the specification does indeed fully enable the amended claims. For example, paragraph 107 of the published application clearly describes the various injection paradigms that can be employed with different forms of botulinum toxin:

> The amount of the Clostridial toxin administered according to a method within the scope of the disclosed invention can vary according to the particular characteristics of the pain being treated, including its severity and other various patient variables including size, weight, age, and responsiveness to therapy. To guide the practitioner, typically, no less than about 1 unit and no more than about 25 units of a botulinum toxin type A (such as BOTOX®) is administered per injection site (i.e. to each muscle portion injected), per patient treatment session. For a botulinum toxin type A such as DYSPORT®, no less than about 2 units and no more about 125 units of the botulinum toxin type A are administered per injection site, per patient treatment session. For a botulinum toxin type B such as MYOBLOC®, no less than about 40 units and no more about 1500 units of the botulinum toxin type B are administered per injection site, per patient treatment session. Less than about 1, 2 or 40 units (of BOTOX®, DYSPORT® and MYOBLOC® respectively) can fail to achieve a desired therapeutic effect, while more than about 25,125 or 1500 units (of BOTOX®, DYSPORT® and MYOBLOC® respectively) can result in significant muscle hypotonicity, weakness and/or paralysis.

Nevertheless, claims 1, 2, 4, 9, 16, and 18 have been amended to specify the type and amount of botulinum toxins claimed, as described in the paragraph quoted above. As such, the Applicants assert that pending claims 1-20 and 29 are fully enabled and respectfully request that the rejections under 35 U.S.C. 112, first paragraph be withdrawn.

2) The Office Action rejects claims 5 and 8 under 35 USC 112, second paragraph, for "failing to particularly point out and distinctly claim the subject matter which Appellant regards as the invention." *See* Office Action at p6. Claim

1 has been amended to remove the term "intradermal" resulting in the claim reading "the method comprising a step of local administration." Support for this amendment can be found in paragraph 87 of the published application.

35 U.S.C. §103 Rejections

1) The Office Action rejects claims 1-3, 10-17, 19-20, and 29 under 35 U.S.C. §103(a) as being unpatentable over Schim (Current Medical Research and Opinion, Vol. 20, No, 1, January 2001, p. 49-53; "Schim") in view of Johnson *et al*. (USP 5,512,547; "Johnson") in view of Cephalalgia, An International Journal of Headache, Volume 24, Supplement 1, 2004 ("Cephalalgia") in view of Aoki *et al*. (USP 6,896,886; "Aoki"). Applicants respectfully traverse this rejection.

To establish a *prima facie* case of obviousness under 35 U.S.C. §103, the Office must meet four conditions. First, the Office must show that the prior art suggested to those of ordinary skill in the art that they should make the claimed composition or device or carry out the claimed process. Second, the Office must show that the prior art itself would have *provided* one of ordinary skill in the art with a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be adequately founded in the prior art and not in an applicant's disclosure. Third, the prior art must teach or suggest all the claim limitations. *In re Vaeck,* 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). Fourth, if an obviousness rejection is based on some combination of prior art references, the Office must show a suggestion, teaching, or motivation to combine the prior art references ("the TSM test"). *In re Dembiczak,* 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). *KSR Int'l Co. v. Teleflex, Inc*., teaches that this fourth prong of the *prima facie* obviousness analysis must not be applied in a rigid or formulaic way such that it becomes inconsistent with the more flexible approach of *Graham v. John Deere*, 383 U.S. 1, 17-18 (1966); 127 S. Ct. 1727 (2007). Nevertheless, the TSM test captures the important insight that "a patent composed of several elements is not proved obvious merely by

demonstrating that each of its elements was, independently, known in the prior art." *Id*. at 1741 (citing *United States v. Adams*, 383 U.S. 39, 50-52 (1966)).

Applicants traverse the rejection. Nevertheless, to expedite prosecution the rejected claims have been amended to include the limitation of claim 4 ("of between about 1 unit and about 1500 units"), which was not subject to the §103 rejection. Therefore, the rejection should be withdrawn.

2) The Office Action rejects claims 1-20, and 29 under 35 U.S.C. §103(a) as being unpatentable over Tepper *et al*. (Cephalalgia, 2003, 23, 581-762; "Tepper") in view of Johnson in view of Cephalalgia, 2004 and further in view of Aoki. Applicants respectfully traverse this rejection.

Tepper, a poster presentation, discusses botulinum toxin administration in the preventative treatment of refractory headaches (treatment of refractory headaches in patients that are medication overusers as well as non-overusers). Unlike the pending claims, Tepper does not suggest methods for treating patients suffering from an acute pain medication overuse disorder, where the patient experiences pain after the intake of acute pain medication. Nor does Tepper teach the use of pure botulinum toxin and further, Tepper does not teach or disclose administration according to the instantly claimed methods, providing no administration information beyond the fact that each patient had received 100 units of botulinum toxin A.

The Office applies Johnson to remedy the absence of teaching related to pure botulinum toxin. While Johnson does teach the use of pure toxin, the reference does not at any point state that the pure toxin is pharmacologically equivalent to the toxin complex used in Tepper. The Office's citing of the supposed advantages displayed by the toxin vice the complex are irrelevant in light of this; possible advantages in shelf life and immunogenicity are of no benefit if the "new" molecule does not perform as well as the "old" molecule, and Johnson provides no indication that the pure toxin works as well as the toxin complex inside the patient. Indeed, Johnson proposes a completely new formulation as compared to the botulinum toxin type A formulation used in

Tepper, one which includes trehalose, and no person of ordinary skill in the art would assume that the pure toxin, with its completely different formulation, would prove as effective pharmacologically as the toxin complex used in Tepper. This shortcoming, especially when combined with Tepper's absolute lack of guidance regarding administration techniques and locations, prevents these references from rendering the pending claims obvious. Neither Cephalalgia, 2004 nor Aoki can remedy this. Both Cephalalgia's teachings regarding diagnostic criteria and Aoki's guidance related to intradermal administration fail to provide the elements lacking in Tepper and Johnson, namely disclosure relating to administration techniques and locations and disclosure relating to the pharmacological effects of pure botulinum toxin vice that of botulinum toxin complex.

Further, a skilled artisan in view of Tepper would likely believe that medication overuse leads to reductions in headache frequency, because Tepper's figure shows there is a lower occurrence of headache in medication "overusers" than "non-overusers" at baseline.

Finally, as stated previously, if an obviousness rejection is based on some combination of prior art references, the Office must show a suggestion, teaching, or motivation to combine the prior art references ("the TSM test"). *In re Dembiczak,* 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). Here, such suggestion is lacking, as Johnson discloses nothing to suggest that pure botulinum toxin is pharmacologically equivalent to the botulinum toxin complex formulation used in Tepper, and one of ordinary skill in the relevant art would never make such an assumption.

Conclusion

For the foregoing reasons, Applicant believes all the pending claims are in condition for allowance and a Notice of Allowance to that effect is respectfully requested. The Commissioner is hereby authorized to charge any additional fees which may be required for entry of this paper, or credit any overpayment, to Deposit Account No. 01-0885. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, the Examiner is kindly urged to call the undersigned at telephone number (714) 246-2842.

Respectfully submitted,

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